EXHIBIT D
Chronology of Significant Activities Regarding IND 36,704 and NDA 21-272 for Remodulin™ (treprostinil sodium) Injection

Date	IND/NDA	Sponsor	Description
April 15, 1991	IND	Burroughs Wellcome	Original IND Application
August 15, 1991	IND	Burroughs Wellcome	Protocol 01 Amendment
August 23, 1991	IND	Burroughs Wellcome	Investigator CV and 1572 Protocol 01
October 28, 1991	IND	Burroughs Wellcome	Investigator CV and 1572 Protocol 01
October 19, 1992	IND	Burroughs Wellcome	IND Annual Report
December 10, 1993	IND	Burroughs Wellcome	IND Annual Report
April 21, 1994	IND	Burroughs Wellcome	Request to place IND on Inactive Status
February 3, 1997	IND	LungRx	Letter regarding transfer from Glaxo Wellcome to LungRX, Inc.
February 14, 1997	IND	LungRx	1st Submission under LungRx – provides for new Protocol P01:01, Investigator's Brochure, Clinical Report, and CV and 1572 for Dr. Rubin
April 15, 1997	IND	LungRx	CMC update/response to FDA questions, Amendment 1 to P01:01, and Investigators 1572 and CVs
June 4, 1997	IND	LungRx	Orphan designation granted for PPH
June 10, 1997	IND	LungRx	Amendment 2 to P01:01
July 18, 1997	IND	LungRx	Amendment 3 to P01:01
August 7, 1997	IND	LungRx	New Protocol P01:02 (PPH), Investigators Badesch, Barst, Brundage, McGoon, Robbins, Rubin and Tapson CVs and 1572s and summary of Toxicology Report on 3-day Rat Infusion
September 12, 1997	IND	LungRx	New Protocol P02:01 (Portopulmonary Hypertension), Investigator Gaine CV and 1572
November 11, 1997	IND	LRX Pharmaceuticals	Correspondence re: 1) inability to develop assay for 15AU81, and 2) PK analysis for P01:02
November 20, 1997	IND	LRX Pharmaceuticals	Company Name change, Amendment 1 to P02:01 adding clinical chemistry profile, including liver function tests and Investigator registrations for Drs. Badesch, Frost, Bourge, McLaughlin, and Brundage
November 21, 1997	IND	LRX Pharmaceuticals	Registration of Investigators Bourge, Frost, and Rich
December 22, 1997	IND	LRX Pharmaceuticals	Amendment 1 for P01:02 (PPH)
December 23, 1997	IND	LRX Pharmaceuticals	New Protocol Submission P03:01(Lower Limb Ischemia), Investigator CV and 1572
January 15, 1998	IND	LRX Pharmaceuticals	Amendment 2 to P02:01, (Portopulmonary Hypertension), modifying exclusion criteria
February 2, 1998	IND	United Therapeutics	Company and Drug Name change, End of Phase II meeting confirmation, Phase III Development Plan
February 3, 1998	IND	United Therapeutics	SAE Report for P01:01 patient 02005
March 13, 1998	NDA	United Therapeutics	Minutes of the February 20, 1998 meeting between FDA and UT
March 16, 1998	IND	United Therapeutics	Amendment 1 to P03:01(PVD/Lower leg Ischemia), modification to 1571 to provide for Dr. McAllister and Dr. Smith for Safety
March 19, 1998	IND	United Therapeutics	IND Annual Report
March 26, 1998	IND	United Therapeutics	Correspondence re: End of Phase II meeting, request for expedited development for PVD
April 7, 1998	IND	United Therapeutics	Pre-Clinical Toxicology Studies: 3-Day Rat; Acute Dose Study in Rat; 14-Day Dose Study in Rat; Acute Dose Study in Beagle Dogs; 14-Day Dose Study in Beagle Dogs;
April 10, 1998	IND	United Therapeutics	New Protocol Submission P01:03 (PPH 8 Week Study), Investigator Registrations Rich, Barst, Bourge, Gaine, and Shapiro
May 12, 1998	IND	United Therapeutics	Amendment 1 of P01:03, providing for addition of blood sample collection as per FDA suggestion
June 17, 1998	IND	United Therapeutics	Amendment 2 of P01:03, providing for new formulations of drug to be used, for dose administration changes, for a pregnancy test in week 8, for three new patients to be included, for vital signs to be collected

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Date	IND/NDA	Sponsor	Description
			during dose optimization and for AEs to be followed to resolution
June 19, 1998	IND	United Therapeutics	CTX Variation (Clinical Trials Exemption)
June 23, 1998	IND	United Therapeutics	New Protocol P01:06 (Continuation Study), Investigator Registration for Drs. Barst, Bourge, Rich and Gaine
July 22, 1998	IND	United Therapeutics	Amendment 3 of P02:01, providing for modification of entry criteria and UT (company's) address change
August 7, 1998	IND	United Therapeutics	P01:02 New Investigator Registration, Dr. Oudiz to replace Dr. Brundage
November 2, 1998	IND	United Therapeutics	New Protocols P01:04 (North American Pivotal) and P01:05 (ROW Pivotal) includes original revision and Amendment 1, Registration of Investigators, and CMC informational amendment providing for the new formulation of UT-15 to be used in the studies
October 26, 1998	IND	United Therapeutics	Amendment 2 to P01:06 , providing to allow an optional hemodynamics and exercise assessment in patients entering this study from P01:03
November 9, 1998	IND	United Therapeutics	Amendment 2 to P01:04 and P01:05, providing for modification of dose regimen, clarification of inclusion/exclusion criteria and amend statistical analysis section to permit second interim efficacy analysis on combined trial data
December 22, 1998	IND	United Therapeutics	Amendment 3 to P01:04 and P01:05 ; providing for the modification of several entry criteria; adding a global quality of life instrument as a secondary efficacy measurement; revising the statistical analysis section; and clarifying certain existing study procedures.
December 29, 1998	IND	United Therapeutics	Amendment 3 to P01:06, providing consistency between this uncontrolled study and two controlled studies, specifically; updated information on drug formulations and storage conditions; a revision in dosing regimen; and additional expected adverse events related to UT-15
February 12, 1999	IND	United Therapeutics	Registration of new P01:05 Investigators for Israeli sites; and registration of P01:06 Investigators
April 15, 1999	IND	United Therapeutics	CMC changes in two volumes, specifically changes to the DS reference standard, synthesis method and analytical controls; DP updated analytical specifications and stability data; and Placebo to include a new specification for metacresol.
May 4, 1999	IND	United Therapeutics	Correspondence requesting meeting regards randomization issues
April 30, 1999	IND	Quintiles	15-Day IND Safety Report
May 5, 1999	IND	United Therapeutics	IND Annual Report
May 7, 1999	IND	United Therapeutics	Drug Product Stability Strategy and request for conference call to discuss stability
May 27, 1999	IND	United Therapeutics	New Protocol P01:07, for conducting the Bioavailability Study (PK)
June 21, 1999	IND	United Therapeutics	Submission of final pre-clinical toxicology and toxicokinetic study reports, in seven volumes
July 7, 1999	IND	United Therapeutics	Submission includes correspondence regarding 7/15/99 meeting with Agency and two certificates of Analysis for lots UT15-99D002 and UT-15-99E001
July 23, 1999	IND	United Therapeutics	Submission of P01:08 protocol, Acetaminophen interaction study with Investigator Data & 1572
July 26, 1999	IND	United Therapeutics	Submission of P01:09 protocol, Chronic PK Study in Health Volunteers with Investigator Data & 1572
August 5, 1999	IND	United Therapeutics	Submission of 7/15/99 FDA mtg. minutes
August 18, 1999	IND	United Therapeutics	Revised Stability Strategy and additional request for approval of 7/15/99 FDA mtg. minutes

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Date	IND/NDA	Sponsor	Description
August 20, 1999	IND	United Therapeutics	Registration of New P01:05 Investigators (North American Sites), CVs &1572s and Investigator's Brochure
September 13, 1999	IND	United Therapeutics	Information Amendment: Chemistry, Manufacturing and Controls: 10.0 mg/mL; HPLC drug product assay method
September 23, 1999	IND	United Therapeutics	New Investigators for P01:05
September 28, 1999	IND	United Therapeutics	Request for Clinical/Nonclinical Pre-NDA Meeting
September 28, 1999	IND	United Therapeutics	Request for CMC Pre-NDA Meeting
October 13, 1999	IND	United Therapeutics	Registration of last 04 investigator's into the 05 study; CVs and 1572s
October 14, 1999	IND	United Therapeutics	Orphan Application Request for Designation for PPH
October 21, 1999	IND	United Therapeutics	Pre-NDA CMC Package Submission
October 27, 1999	IND	United Therapeutics	Pre-NDA Clinical/Nonclinical Package
November 2, 1999	IND	United Therapeutics	Orphan Designation Approved
November 10, 1999	IND	United Therapeutics	Amendment 4 to P01:06 providing for Portopulmonary Hypertension and HIV patients
December 6, 1999	NDA	United Therapeutics	Minutes of the November 15, 1999 Pre-NDA meeting between FDA and UT
December 7, 1999	IND	United Therapeutics	Toxicology Submission, 6 month dog continuous subcutaneous infusion of UT-15
December 14, 1999	IND	Quintiles	15 Day Safety Report
December 13, 1999	IND	United Therapeutics	Response to CMC pre-NDA meeting minutes
January 3, 2000	IND	United Therapeutics	New Protocol P01:10 (Mass Balance Radio-label Study) and CMC amendment for radio label batch
January 6, 2000	IND	United Therapeutics	New Protocol P01:11 – Compassionate use study in transition from IV Flolan to Subcutaneous UT-15
January 17, 2000	IND	United Therapeutics	Pre-NDA Clinical-Nonclinical Mtg. Minutes
January 19, 2000	IND	United Therapeutics	Statistical Analysis Plan
February 1, 2000	IND	Quintiles	15-Safety Report (from Quintiles)
February 2, 2000	IND	United Therapeutics	Carcinogenicity Rationale
February 9, 2000	IND	United Therapeutics	Amendment 5 to P01:06
February 10, 2000	IND	United Therapeutics	Nonclinical Amendment Toxicology and PK Studies in 4 volumes
February 18, 2000	IND	Quintiles	IND Safety Report SAE Report
February 18, 2000	IND	United Therapeutics	Protocol Amendment Revision to Amendment 5 to P01:06
March 6, 2000	IND/NDA	United Therapeutics	Statistical Analysis Plan, final review before unblinding
March 23, 2000	IND/NDA	United Therapeutics	Final Statistical Analysis Plan Issues for P01:04 and P01:05 (SER072)
April 11, 2000	NDA	United Therapeutics	Letter regarding exemption from conducting carcinogenicity studies
April 17, 2000	NDA	United Therapeutics	Confirmation of Presubmission of NDA
April 28, 20	IND	United Therapeutics	1999-2000 IND Annual Report
May 5, 2000	IND	United Therapeutics	Amendment # 1 to Protocol P01:11 to allow patients to transition to UT-15 from Flolan
May 18, 2000	IND	United Therapeutics	Amendment #6 to Protocol P01:06 to allow thromboembolic patients
June 6, 2000	IND	United Therapeutics	New Protocol P01:12 – Subcutaneous Infusion of UT-15 Therapy on Single-Dose Warfarin Pharmacodynamics and Pharmacokinetics in Healthy Patients.
June 29, 2000	IND	United Therapeutics	IND Safety Report – P01:06 Anaemia, Israel site 57; Patient # 557005
August 11, 2000	NDA	United Therapeutics	Partial NDA submission - CMC and Item 5 Volumes to FDA (35 total; vol 1.1-1.35)
September 26, 2000	IND	United Therapeutics	New Investigators – P01:11 Nicholas S. Hill, MD; Prof. T.W. Higenbottam; Ronald J. Oudiz, MD; David Dunbar Ivy, MD
July 3, 2000	IND	United Therapeutics	IND Safety Report Follow-up P01:06 Anemia, Patient 557005
October 13, 2000	NDA	United Therapeutics	Synquest (UT Chicago) Acceptable Inspection notification

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Date	IND/NDA	Sponsor	Description
October 16, 2000	NDA	United Therapeutics	Remaining NDA documents submitted to FDA; Vol 2.1 to 2.69
October 16, 2000	IND/NDA	United Therapeutics	Name change from Uniprost to Remodulin
October 19, 2000	NDA	United Therapeutics	Letter from FDA confirming receipt of NDA on October 16, 2000
October 23, 2000	NDA	United Therapeutics	Response to FDA request for microbiology information
October 25, 2000	IND	United Therapeutics	Registration of New Investigators of P01:06 Study (Zwicke; Lawrence)
October 31, 2000	IND	United Therapeutics	IND Safety Report
November 3, 2000	NDA	United Therapeutics	P01:04/05: DSMB and Steering Committee Summary results
November 10, 2000	NDA	United Therapeutics	P01:04/05: Information requested for statistician
November 10, 2000	NDA	United Therapeutics	Response to FDA request. List of microbial deficiencies provided.
November 13, 2000	NDA	United Therapeutics	P02:01: Information for Dr. Nguyen and water injection diagram
November 16, 2000	NDA	United Therapeutics	Information for clinical sites 02 (Barst), 09 (Frost) and 10 (Bourge)
November 16, 2000	NDA	United Therapeutics	CRFs requested by Dr. Stockbridge P01:04: 23002 and 09001 P01:05: 50013
November 28, 2000	IND	United Therapeutics	IND Safety Report
November 30, 2000	IND	United Therapeutics	IND Safety Report
November 30, 2000	IND	United Therapeutics	IND Safety Report
November 30, 2000	IND	United Therapeutics	IND Safety Report
December 1, 2000	NDA	United Therapeutics	P01:06: Interim Study Updated for Volume 2.51 of the NDA submitted September 15, 2000, page 13789, lab data
December 1, 2000	IND	United Therapeutics	Registration of New Investigators of P01:06 Study (Waxman, Edelman, Granton, Shardonofsky)
December 4, 2000	NDA	United Therapeutics	CMC Background information for the December 7, 2000 meeting
December 7, 2000	NDA	United Therapeutics	CMC: December 7th minutes and response regarding starting materials for the API synthesis
December 14, 2000	NDA	United Therapeutics	Correspondence regarding not presenting to the Cardio Renal Drug Products Committee in February Advisory Committee
December 22, 2000	NDA	United Therapeutics	Response to FDA request – Starting materials for API synthesis.
December 22, 2000	NDA	United Therapeutics	CMC: Updated Stability Data for 10 mg/mL strength
January 4, 2001	IND	United Therapeutics	Registration of New Investigator of P01:06 Study (Ross)
January 5, 2001	NDA	United Therapeutics	Letter to request meeting on January 25, 2001 to discuss clinical issues
January 5, 2001	NDA	United Therapeutics	Response to FDA request – Classification of 18 discontinued patients in P01:04/05
January 11, 2001	NDA	United Therapeutics	Additional information on patients in P01:04/05 Pivotal Studies regarding discontinuations due to AEs
January 18, 2001	IND	United Therapeutics	IND Safety Report
January 23, 2001	NDA	United Therapeutics	Agenda and package for the January 25, 2001 Clinical and PK meeting with FDA
January 25, 2001	NDA	United Therapeutics	Submission of P01:12
February 2, 2001	MAA	United Therapeutics	MAA submitted
February 2, 2001	IND	United Therapeutics	Registration of New Investigators P01:06 (Gibbs)
February 2, 2001	NDA	United Therapeutics	Response to Steering Committee queries and January 25, 2001 call with Dr. Karkowsky
February 6, 2001	NDA	United Therapeutics	Final Minutes of January 25, 2001 meeting between FDA and UT
February 9, 2001	NDA	United Therapeutics	Call from Dr. Karkowsky requesting information and clarification on several issues
February 15, 2001	NDA	United Therapeutics	Response to request for information regarding the January 25th meeting. Telephone conversation with Dr. Karkowsky on February 9, 2001 for additional information to complete the review.
February 15, 2001	NDA	United Therapeutics	120-Day Safety Update (Volumes 3.1 to 3.12)
February 15, 2001	NDA	United Therapeutics	Response to FDA request for information. SAS Data Sets for Safety

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Date	IND/NDA	Sponsor	Description
			Update for P01:06 on CD for 120-Day Safety Report Update. Hardcopy of annotated CRFs also endlosed
February 19, 2001	NDA	United Therapeutics	Response to FDA request for information. Microbial deficiences regarding the 11/6/00 letter. Reference to 11/10/00 response to issues. Telephone conversation with Drs Langille and Cooney on 2/1/01. Telephone conversation regarding hand stoppering of vials (from 11/10/00 response).
February 23, 2001	NDA	United Therapeutics	Response to FDA request for information. CMC Amendment of updated stability
February 23, 2001	IND	United Therapeutics	IND Safety Report Follow-up
February 26, 2001	NDA	United Therapeutics	Diskette and hard copy of draft labeling. Also incorporation of new trade name Remodulin.
February 28, 2001	NDA	United Therapeutics	PK Amendment: Response to FDA request. P01:12 Warfarin Interaction Study tables and listings.
February 28, 2001	NDA	United Therapeutics	CMC Amendment regarding specifications and testing for UT-15. Discussion of changes to drug substance and drug product specifications (97W86; 751W93; 1AU90).
March 1, 2001	NDA	United Therapeutics	CMC Amendment regarding specifications and testing for UT-15. Amendment committing to changes to drug substance and drug product specifications. Also revised test methods of drug substance and drug product specifications
March 12, 2001	NDA	United Therapeutics	Meeting with FDA regarding NDA issues
April 4, 2001	NDA	United Therapeutics	Briefing Document for April 11, 2001 meeting
April 9, 2001	NDA	United Therapeutics	Briefing Document addendum with completers analysis of walk
April 11, 2001	NDA	United Therapeutics	Meeting with FDA regarding analysis of P01:04/05 data combining exercise tolerance with Borg Dyspnea scores
April 12, 2001	NDA	United Therapeutics	Amendment to pending application – additional statistical analyses exercise and Borg Dyspnea scores in P01:04/05
April 12, 2001	IND	United Therapeutics	IND Safety Report
April 24, 2001	IND	United Therapeutics	Registration of New Investigators of P01:06 Study (Pepke-Zaba, Boonstra)
May 9, 2001	IND	United Therapeutics	P01:06 Amendment 7- Extension of the chronic treatment phase of the study from 3 to 5 years
May 14, 2001	NDA	United Therapeutics	Amendment to pending application - additional analyses provided to support the NDA
June 14, 2001	NDA	United Therapeutics	Amendment to pending application – Nonproprietary name change of Remodulin Injection from treprostinol to treprostinil
June 14, 2001	NDA	United Therapeutics	Amendment to pending application – CMC amendment
June 22, 2001	NDA	United Therapeutics	Meeting with FDA to discuss Benefits-to-Risk profile of Remodulin
June 25, 2001	NDA	United Therapeutics	Amendment to pending application – Follow-up document to outline the Benefits-to-Risk profile of Remodulin
July 5, 2001	NDA	United Therapeutics	NDA withdrawn for resubmission at a later date
August 9, 2001	NDA	United Therapeutics	Cardiovascular and Renal Drugs Advisory Committee recommending approval of Remodulin by a 6-3 vote. NDA resubmitted.
August 16, 2001	NDA	United Therapeutics	Amendment to pending application – additional analyses submitted following advisory committee
August 20, 2001	IND	United Therapeutics	IND Safety Report
September 24, 2001	NDA	United Therapeutics	Amendment to pending application – Further docmentation supporting the Benefits-to-Risk profile of Remodulin
September 27, 2001	IND	United Therapeutics	Registration of New Investigator of P01:06 Study (Kiely)
September 28, 2001	IND	United Therapeutics	IND Safety Report

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Date	IND/NDA	Sponsor	Description
October 2, 2001	NDA	United Therapeutics	Amendment to pending application – Summary comparison of Remodulin vs Bosentan
October 5, 2001	IND	United Therapeutics	IND Safety Report
October 30, 2001	NDA	United Therapeutics	Request submitted for priority evaluation status of Remodulin
November 1, 2001	NDA	United Therapeutics	Amendment of pending application – submission of USAN "Statement on a Nonproprietary Name Adopted by the USAN Council"
November 13, 2001	IND	United Therapeutics	IND Safety Report
December 17, 2001	IND	United Therapeutics	Annual Report for Feb 2000 to Feb 2001
December 13, 2001	NDS	United Therapeutics	Canada – New Drug Submission
February 8, 2002	NDA	United Therapeutics	Approvable letter issued for Remodulin
February 8, 2002	IND	United Therapeutics	IND Safety Report
February 13, 2002	NDA	United Therapeutics	Meeting with FDA to discuss Approvable Letter requirements
February 13, 2002	NDA	United Therapeutics	Response to Approvable Letter - Submission of vial and carton labels
February 25, 2002	NDA	United Therapeutics	Submission of postmarketing protocol P01:13
February 28, 2002	NDA	United Therapeutics	Submission of P01:13 informed consent
March 1, 2002	NDA	United Therapeutics	Request for CMC clarification
March 7, 2002	NDA	United Therapeutics	Meeting with FDA to discuss P01:13
March 14, 2002	NDA	United Therapeutics	CMC Amendment- updated stability commitment statement
March 20, 2002	NDA	United Therapeutics	Complete Response to Approvable Letter and submission of final printed label (package insert)
April 1, 2002	NDA	United Therapeutics	Class 1 Complete Response Resubmission: Final Response to Approvable Letter
April 9, 2002	NDA	United Therapeutics	CMC Amendment
April 19, 2002	IND	United Therapeutics	Annual Report for Feb 11, 2001 – Feb 10, 2002 and Updated Investigator's Brochure
May 21, 2002	NDA	United Therapeutics	Approval letter issued for Remodulin